**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

| | | | | |
|---|---|---|---|---|
| Applicant(s) | : | PEPYS | | |
| Serial No. | : | 09/737,544 | Filed : | December 18, 2000 |
| For | : | TREATMENT AND PREVENTION OF TISSUE DAMAGE | | |
| Examiner | : | Shengjun Wang | | |
| Art Unit | : | 1617 | Confirmation No. : | 1521 |

745 Fifth Avenue, New York, NY 10151

**FILED VIA EFS-WEB**
**ON SEPTEMBER 5, 2007**

**TRANSMITTAL OF DECLARATION OF DR. JON COOPER**

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450
Dear Sir:

Further to the Amendment filed August 31, 2007, submitted herewith is the Declaration of Dr. Jon Cooper. Please consider this Declaration with the Amendment, and PowerPoint presentations filed on August 31, 2007, along with the matters discussed during the August 14, 2007 interview. In view of the amendments and remarks of the August 31, 2007 Amendment, the matters discussed during the interview (for which the Examiner and SPE are thanked for the courtesies extended), and the PowerPoint presentations then presented (which were also filed August 31, 2007), the application is in condition for allowance. Reconsideration and withdrawal of the rejections of the application, early and favorable reconsideration of the application, and prompt issuance of a Notice of Allowance are respectfully requested.[1]

Respectfully submitted,
FROMMER LAWRENCE & HAUG LLP

By: /Thomas J. Kowalski/
Thomas J. Kowalski, Reg. No. 32,147
Angela M. Collison, Reg. No. 51,107
(212) 588-0800

[1] The Examiner is also again asked to please, as discussed during the interview, work with Applicant's attorney during September 2007 to reach agreement on allowable subject matter on or before September 30, 2007). Applicant's Attorneys will contacting the Examiner pursuant to that discussion and request.

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

| | | |
|---|---|---|
| Applicant(s) | : | PEPYS |
| Serial No. | : | 09/737,544 |
| For | : | TREATMENT AND PREVENTION OF TISSUE DAMAGE |
| Filed | : | December 18, 2000 |
| Examiner | : | Shengjun Wang |
| Art Unit | : | 1617 |
| Confirmation No. | : | 1521 |

745 Fifth Avenue, New York, NY 10151

**FILED VIA EFS-WEB**
**ON SEPTEMBER 5, 2007**

## DECLARATION OF DR. JON COOPER

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450
Dear Sir:

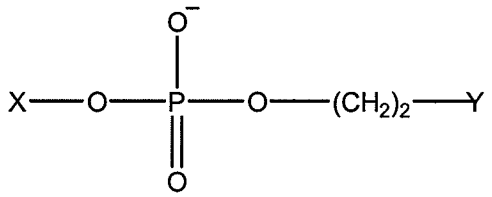
Dr. Jon Cooper declares and says that:

1. My Curriculum vitae is attached to this Declaration, and incorporated herein by reference.

2. I understand that the above-captioned patent application calls for a method for reducing damage to heart muscle caused by C-reactive protein (CRP) in a patient who has suffered ischemic necrosis and is in need thereof, comprising inhibiting CRP binding to its ligands *in vivo* in the patient, by administering to the patient an effective amount of a compound that comprises phosphocholine or a derivative thereof.

3. I also understand that the above-captioned patent application calls for a method for reducing tissue damage, e.g., ischemic necrosis or stroke, caused by C-reactive protein (CRP) in a patient in need thereof who has suffered an inflammatory or tissue damaging condition comprising inhibiting CRP binding to its ligands *in vivo* within the patient, by administering to the patient an effective amount of a compound that comprises phosphocholine or a derivative thereof.

4. I further understand, for example, that that the compound can have the general formula (II)



(II)

wherein X is H or $C_1$ to $C_{20}$, e.g., $C_l$ to $C_{20}$ alkyl or $C_{l2}$ to $C_{20}$ alkyl, and Y is N substituted to form ammonium.

5. I additionally understand that Yedgar (US5,064,817) has been cited by the US Patent and Trademark Office (USPTO) against the above-captioned patent application. I have reviewed and have familiarity with Yedgar, as well as with the above-captioned patent application; and also have an understanding as to CRP and CRP binding to its ligands *in vivo*. Therefore, based on my education, training and experience and that which I have reviewed and am familiar with, and my understandings, I respectfully submit that I am qualified to make this Declaration.

6. I respectfully assert that Yedgar compounds would not be suitable for inhibiting CRP binding to its ligands *in vivo* in a patient through administration thereof to the patient because of the size of the Yedgar compounds. In particular, please note that Yedgar compounds include a carrier. The carriers can have a wide range of molecular weight, e.g., above 50,000 (up to a few hundred thousands); see, e.g., Yedgar, col. 4, lines 60-68. Therefore, in my view, Yedgar does not teach or suggest a compound suitable for inhibiting CRP binding to its ligands *in vivo* in a patient through administration thereof to the patient.

7. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful statements may jeopardize the validity of the application or any patent issued thereon.

Dated: 2/9/07 By: J. Cooper.
Dr. Jon Cooper

## Jonathan B. Cooper – Curriculum Vitae

Jon Cooper is a Reader in the School of Biological Sciences at the University of Southampton who specialises in expression and X-ray structure analysis of proteins including calcium-signalling proteins, components of bacterial secretion systems, aspartic proteinases and enzymes of tetrapyrrole biosynthesis. He teaches structural biology on undergraduate programmes and at the post-graduate level. He has 22 years of experience in the protein crystallography field. He is a member of Biological Structures Group of the British Crystallographic Association (BCA), the Tetrapyrrole Discussion Group and is a tutor at the BCA Protein Crystallography Summer School (held in Bristol and, most recently, in Oxford, 2006). He has been a member of the Life Science Review Committee at the European Synchrotron Research Facility (ESRF) Grenoble. He acted as guest editor for an issue of the journal Current Drug Targets: volume 5 (2004) which was dedicated to structure-based drug design. He has been the external examiner for the BSc in Molecular Biology at Birkbeck College, University of London and he examines around 3 PhD thesis candidates per annum. He acts as referee for around 5-6 journal publications per annum. In 1993, he was awarded the Rosalind Franklin Prize for research at Birkbeck College London.

He acted as local organiser for the Biological Structures Group (BSG) sessions at the BCA Spring Meeting in 2001 (Reading). He organised the South-West Structural Biology Consortium (SWSBC) meeting which was hosted in Southampton in April 2004 and was attended by around 70 participants. He has chaired sessions at the BCA Spring and Winter Meetings 2006 (in Lancaster and Birmingham, respectively.) as well as the SWSBC meetings in Southampton (April 2004) and Bath (April 2006).

### Degrees:

BA (Hons) Biochemistry (Oxford) 1985 (2.1).
PhD Crystallography (Birkbeck College, University of London) 1989.

### Posts held:

PhD student 1985-1988, Department of Crystallography, Birkbeck College London.
Research Assistant 1988-1989, Department of Crystallography, Birkbeck College London.
Research Fellow, 1989-1991, ICRF Unit, Birkbeck College London.
Lecturer, 1991-1996, Department of Crystallography, Birkbeck College London.
Lecturer, 1996-2001, School of Biological Sciences, University of Southampton.
Senior Lecturer, 2001-2005, School of Biological Sciences, University of Southampton.
Reader, 2005- , School of Biological Sciences, University of Southampton.

### Grants active since 2001:

Prof. P.M.Shoolingin-Jordan and Dr J.B.Cooper.
X-ray structure based investigations on the mechanism of pyrrole synthesis catalysed by E. coli 5-aminolaevulinic acid dehydratase.
BBSRC
£206,846
1/9/98-31/08/01

Dr J.B.Cooper, Prof. S.P.Wood and Prof. C.Anthony.
A study of protein-protein interactions and electron transfer: structure and interactions of an unusual c-type cytochrome.
BBSRC
£200,300
22/02/00-21/02/03

Dr J. B. Cooper, Prof. M. J. Warren and Prof. P. M. Shoolingin-Jordan.
X-ray structural studies of substrate binding and mechanism of 5-aminolaevulinic acid dehydratase.
BBSRC
£180,112
1/11/00-1/11/03

Dr J. B. Cooper, Dr M. P. Crump and Prof. S. P.Wood.
Atomic resolution X-ray, neutron and NMR studies of aspartic proteinase structure and function.
BBSRC
£195,048
2001-2004.

Dr J. B. Cooper, Dr D. J. Hopper and Prof. S. P. Wood.
Structure and function of a novel dioxygenase.
BBSRC
£56,204
2003-2004.

Professor G. G. Kneale and Dr J. B. Cooper.
The structural basis of gene regulation in a novel restriction-modification system.
BBSRC
£208,453
2003-2006.

Prof. S. P. Wood, Dr A. R. Coker and Dr J. B. Cooper.
Structure and mechanism of the C-C hydrolases: investigation of a non-nucleophilic mechanism.
BBSRC
£122,516
2003-2005.

Professor W. Fuller, Dr D. J. Barlow, Dr J. B. Cooper, Dr V. T. Forsyth, Professor G. Kneale, Professor M. J. Lawrence, Professor R. N. Perham, Dr O. Byron, Professor A. Watts, Professor N. Isaacs.
Deuteration initiative for biological neutron scattering and NMR.
£800,878 (grant administered by the University of Keele).
2003-2005.

Professor W. Fuller, Professor JG Lindsay, Dr D Barlow, Dr J Cooper, Professor GG Kneale, Professor ED Laue, Professor MJ Lawrence, Dr DA Marvin, Dr O Byron, Professor A Watts, Professor NW Isaacs, Professor CJ Cardin.
Deuteration Initiative for Neutron Scattering and NMR Studies of Biological Molecules.
£691,468 (grant administered by the University of Keele).
2006-2009.

**Publications in last 3 years**:

High resolution structure of BipD: An invasion protein associated with the type III secretion system of *Burkholderia pseudomallei*. Erskine, P.T., Knight, M.J., Ruaux, A., Mikolajek, H., Wong Fat Sang, N., Withers, J., Gill, R., Wood, S. P., Wood, M., Fox, G. C. and Cooper, J. B. (2006). J. Molec. Biol. 363,125-136.

X-ray, neutron and NMR studies of the catalytic mechanism of aspartic proteinases. Coates, L., Erskine, P.T., Mall, S., Gill, R., Wood, S.P., Myles, D.A.A., Cooper, J.B. (2006). Eur. Biophys. J. Biophys. Lett. 35, 559-566.

Crystallization and preliminary X-ray diffraction analysis of BipD, a virulence factor from *Burkholderia pseudomallei*. Knight, M. J., Ruaux, A., Mikolajek, H., Erskine, P. T., Gill, R., Wood, S. P., Wood, M. and Cooper, J. B. (2006). Acta Crystallogr. F62: 761-764.

The molecular basis of heme oxygenase deficiency in the pcd1 mutant of pea. Linley, P. J., Landsberger, M., Kohchi, T., Cooper, J. B. and Terry, M. J. (2006). FEBS J. 273, 2594-2606.

The 1.6 Å X-ray structure of the unusual c-type cytochrome, cytochrome $c_L$, from the methylotrophic bacterium *Methylobacterium extorquens*. Williams, P., Coates, L., Mohammed, F., Gill, R., Erskine, P., Bourgeois, D., Wood, S. P., Anthony, C. and Cooper, J. B. (2006) J. Molec. Biol. 357, 151-162.

Structure of the neuronal protein calexcitin suggests a mode of interaction in signalling pathways of learning and memory. Erskine, P. T., Beaven, G. D. E., Hagan, R., Findlow, I. S., Werner, J. M., Wood, S. P., Vernon, J., Giese, K. P., Fox, G. C. and Cooper, J. B. (2006) J. Molec. Biol. 357, 1536-1547.

Structure of yeast 5-aminolaevulinic acid dehydratase complexed with the inhibitor 5-hydroxylaevulinic acid. Erskine, P. T., Coates, L., Newbold, R., Brindley, A. A., Stauffer, F., Beaven, G. D. E., Gill, R., Coker, A., Wood, S. P., Warren, M. J., Shoolingin-Jordan, P. M., Neier, R., Cooper, J. B. (2005) Acta Crystallogr. D61, 1222-1226.

The X-ray structure of *Chlorobium vibrioforme* 5-aminolaevulinic acid dehydratase complexed with a diacid inhibitor. Coates, L. Beaven, G., Erskine, P. T., Beale, S., Wood, S. P., Shoolingin-Jordan, P. M. and Cooper, J. B. (2005) Acta Crystallogr. D61, 1594-1598.

Crystallisation and preliminary X-ray diffraction analysis of calexcitin from *Loligo pealei* - a neuronal protein implicated in learning and memory. Beaven, G. D. E., Erskine, P. T., Wright, J. N., Mohammed, F., Gill, R., Wood, S. P., Vernon, J., Giese, K. P. and Cooper, J. B. (2005) Acta Crystallogr. F61, 879-881.

High resolution structure of myo-inositol monophosphatase; the target of lithium therapy. Gill, R., Mohammed, F., Badyal, R., Coates, L., Erskine, P. T., Thompson, D., Cooper, J. B., Gore M. G. and Wood, S. P. (2005) Acta Crystallogr. D61, 545-555.

The structure of the C-C bond hydrolase MhpC provides insights into its catalytic mechanism. Dunn, G., Montgomery, M. G., Mohammed, F., Coker, A., Cooper, J. B., Robertson, T., Garcia, J. L., Bugg T. D. H. and Wood, S. P. (2005) J. Molec. Biol. 346, 253-2651.

The atomic resolution structure of methanol dehydrogenase from *Methylobacterium extorquens*. Williams, P. A., Coates, L., Mohammed, F., Gill, R., Erskine, P. T., Coker, A., Wood, S. P., Anthony, C. and Cooper, J. B. (2005) Acta Crystallogr. D, D61, 75-79.

Crystallization and preliminary X-ray analysis of the controller protein C.Ahdl from *Aeromonas hydrophilia*. McGeehan, J. E., Streeter, S., Cooper, J. B., Mohammed, F., Fox, G. C., Kneale, G. G. (2004) Acta Crystallogr. D 60, 323-325.

Crystallization and X-ray analysis of the Y75N mutant of *Mucor pusillus* pepsin complexed with inhibitor PD-135,040 at 1.37 Ångstrom. Badasso, M. O., Dhanaraj, V., Wood, S. P., Cooper, J. B., Blundell, T. L. (2004) Acta Crystallogr. D 60, 770-772.

The X-ray structure of the plant like 5-aminolaevulinic acid dehydratase from *Chlorobium vibrioforme* complexed with the inhibitor laevulinic acid at 2.6 Ångstrom resolution. Coates, L., Beaven, G., Erskine, P. T., Beale, S. I., Avissar, Y. J., Gill, R., Mohammed, F., Wood, S. P., Shoolingin-Jordan, P., Cooper, J. B. (2004) J. Molec. Biol. 342, 563-570.

**Previous publications (from 1987-2003)**:

J.B.Cooper, S.I.Foundling, A.Hemmings, F.E.Watson, B.L.Sibanda, T.L.Blundell, D.M.Jones, A.Hallett, B.Atrash and M.Szelke. 'Inhibitors of aspartic proteinases and their relevance to the design of antihypertensive agents'. Biochem. Soc. Trans. (1987) 15, 751 754.

Jon Cooper, Steve Foundling, Andrew Hemmings, Tom Blundell, D.Michael Jones, Allan Hallett and Michael Szelke. 'The structure of a synthetic renin inhibitor complexed with endothiapepsin'. Eur.J.Biochem. (1987) 169, 215 221.

S.I.Foundling, J.B.Cooper, F.E.Watson, A.Cleasby, L.H.Pearl, B.L.Sibanda, A.M.Hemmings, S.P.Wood, T.L.Blundell, M.J.Valler, C.G.Norey, J.Kay, J.Boger, B.Dunn, M.Leckie, D.M.Jones, B.Atrash, A.Hallett, M.Szelke. 'High resolution X ray analyses of renin inhibitor aspartic proteinase complexes'. Nature (1987) 327, 349 352.

T.L.Blundell, J.B.Cooper, S.I.Foundling, D.M.Jones, B.Atrash, M.Szelke. 'On the rational design of renin inhibitors: X ray studies of aspartic proteinases complexed with transition state analogues'. Biochemistry (1987) 26, 5585 5590.

S.I.Foundling, J.B.Cooper, F.E.Watson, L.H.Pearl, A.M.Hemmings, S.P.Wood, T.L.Blundell, A.Hallett, D.M.Jones, J.Sueiras, B.Atrash and M.Szelke. 'Crystallographic studies of reduced bond renin inhibitors complexed with an aspartic proteinase'. J.Cardiovascular Pharmacol.(1987) 10 (Suppl.7), 559 568.

J.B.Cooper and C.J.Harris. 'Current directions in renin inhibition'. Curr.Cardiovasc.Patents (1988) 1(2), 143 157.

J.B.Cooper, S.I.Foundling, T.L.Blundell, J.Boger, R.Jupp and J.Kay. 'X ray studies of aspartic proteinase statine inhibitor complexes'. Biochemistry (1989) 28, 8596 8603.

A.Sali, B.Veerapandian, J.B.Cooper, S.I.Foundling, D.J.Hoover and T.L.Blundell. 'High resolution X ray diffraction study of the complex between endothiapepsin and an oligopeptide inhibitor: the analysis of the inhibitor binding and description of the rigid body shift in the enzyme'. EMBO Journal (1989) 8(8), 2179 2188.

T.L.Blundell, J.A.Jenkins, B.T.Sewell, L.H.Pearl, J.B.Cooper, I.J.Tickle, B.Veerapandian and S.P.Wood. 'X ray analysis of Aspartic Proteinases I. The three dimensional structure at 2.1 Ångstroms of endothiapepsin'. Journal of Molecular Biology (1990) 211, 919 941.

J.B.Cooper, G.Khan, G.Taylor, I.J.Tickle and T.L.Blundell. 'X ray Analyses of Aspartic Proteinases II. Three dimensional structure of the hexagonal crystal form of porcine pepsin at 2.3 Ångstroms resolution'. Journal of Molecular Biology (1990) 214, 199 222.

B.Veerapandian, J.B.Cooper, A.Sali and T.L.Blundell. 'X ray analysis of Aspartic Proteinases III. The three dimensional structure of endothiapepsin complexed with a transition state isostere of renin at 1.6 Ångstroms resolution'. Journal of Molecular Biology (1990), 216, 1017 1029

A.Sali, B.Veerapandian, J.B.Cooper, T.Hofmann and T.L.Blundell. 'Domain Flexibility in Aspartic Proteinases'. Proteins (1992) 12, 158 170.

M.Badasso, C.Frazao, B.L.Sibanda, V.Dhanaraj, C.DeAlwis, J.B.Cooper, S.P.Wood and T.L.Blundell. 'Crystallization and Preliminary X ray Analysis of Complexes of Peptide Inhibitors with Human Recombinant and Mouse Submandibular Renins'. J.Mol.Biol. (1992) 223, 447 453.

S.P.Wood, J.B.Cooper, G.Louie, P.Brownlie, R.Lambert, T.L.Blundell, M.Warren and P.M.Jordan. 'Crystallization and Preliminary X ray Investigation of E.Coli Porphobilinogen Deaminase.' J.Mol.Biol. (1992) 224, 269 271.

M.Badasso, B.L.Sibanda, J.B.Cooper, C.G.Dealwis and S.P.Wood. 'Crystal quality and inhibitor binding by aspartic proteinases; preparation of high quality crystals of mouse renin'. J.Cryst.Growth (1992) 122, 393-399.

J.E.Pitts, V.Dhanaraj, C.G.Dealwis, D.Mantafounis, P.Nugent, P.Oprayoon, J.B.Cooper, M.Newman and T.L.Blundell. 'Multidisciplinary cycles for protein engineering: site directed mutagenesis and X-ray structural studies of aspartic proteinases'. Scand.J.Clin.Invest. (1992) 52, 39-50.

B.Veerapandian, J.B.Cooper, A.Šali and T.L.Blundell, R.L.Rosati, B.W.Dominy, D.B.Damon, and D.J.Hoover. 'Direct observation by X ray analysis of the tetrahedral "intermediate" of aspartic proteinases'. Protein Science (1992) 1, 322 328.

V.Dhanaraj, C.G.Dealwis, C.Frazao, M.Badasso, B.L.Sibanda, I.J.Tickle, J.B.Cooper, H.P.C.Driessen, M.Newman, C.Aguilar, S.P.Wood, T.L.Blundell, P.M.Hobart, K.F.Geohegan, M.J.Amirati, D.E.Danley, B.A.O'Connor and D.J.Hoover. 'X ray analyses of peptide inhibitor complexes define the structural basis of specificity for human and mouse renins'. Nature (1992) 357, 466 472.

J.Cooper, W.Quail, C.Frazao, S.I.Foundling and T.L.Blundell. 'X-ray crystallographic analysis of the inhibition of endothiapepsin by cyclohexyl renin inhibitors'. Biochemistry (1992) 31, 8142-8150.

Louie GV, Brownlie PD, Lambert R, Cooper JB, Blundell TL, Wood SP, Warren MJ, Woodcock SC and Jordan PM. 'Structure of porphobilinogen deaminase reveals a flexible multidomain polymerase with a single catalytic site'. Nature (1992) 359, 33-39

C.F.Aguilar, M.P.Newman, J.B.Cooper, I.J.Tickle, and T.L.Blundell and J.Sanz-Aparicio. 'The use of protein homologues in the rotation function'. Acta Cryst. (1993) A49 306-315.

M.Badasso, S.P.Wood, C.F.Aguilar, J.B.Cooper, T.L.Blundell and T.Dreyer. 'Crystallisation and preliminary crystallographic characterisation of aspartic proteinase-A from Baker's Yeast and its complexes with inhibitors'. J.Mol.Biol. (1993) 232, 701-703.

M.Badasso, J.B.Cooper, C.Dealwis, B.A.Wallace, E.A.Lunney, H.W.Hamilton, J.C.Hodges, J.S.Kaltenbronn, J.T.Repine, W.T.Lowther, B.M.Dunn and C.Humblet. 'Analyses of ligand binding in five endothiapepsin crystal complexes and their use in the design and evaluation of novel renin inhibitor'. J.Med.Chem. (1993) 36, 3809-3820.

D.Bailey, J.B.Cooper, T.L.Blundell, B.Veerapandian, B.Atrash, D.M.Jones and M.Szelke. 'X-Ray crystallographic studies of complexes of pepstatin A and a statine-containing human renin inhibitor with endothiapepsin'. Biochem.J. (1993) 289, 363-371.

M.Badasso, J.B.Cooper, I.J.Tickle, H.Driessen, T.L.Blundell, C.G.Dealwis, C.Frazao, K.Murakami, J.Miyazaki, J.Sueiras-Diaz, D.M.Jones and M.Szelke. 'X-ray analysis at 2.0Å resolution of mouse submaxillary renin complexed with a decapeptide, inhibitor CH-66, based on the 4-16 fragment of rat angiotensinogen'. J.Mol.Biol. (1994) 236, 342-360.

J.B.Cooper and D.Bailey. 'A structural comparison of 21 inhibitor complexes of the aspartic proteinase from Endothia parasitica'. Protein Science (1994) 3, 2129-2143.

J.B.Cooper, H.Driessen, S.P.Wood, Y.Zhang, and D.Young. 'Crystallisation and preliminary X-ray analysis of the superoxide dismutase from Mycobacterium tuberculosis'. J.Mol.Biol. (1994) 235, 1156-1158.

P.D.Brownlie, R.Lambert, G.V.Louie, P.M.Jordan, T.L.Blundell, M.J.Warren, J.B.Cooper, and S.P.Wood. 'The three-dimensional structures of mutants of porphobilinogen deaminase: Toward an understanding of the structural basis of acute intermittent porphyria'. Prot.Sci. (1994) 3, 1644-1650.

J.B.Cooper, A.J.Beveridge, and C.Dealwis. 'A theoretical study of the active site complexes formed between endothiapepsin and three potent inhibitors: Pepstatin A, and peptide analogues containing difluorostatone and phosphostatine. Implications for inhibitor design'. Theo Chem (1995) 333, 87-97.

J.B.Cooper, K.McIntyre, M.O.Badasso, S.P.Wood, Y.Zhang, T.R.Garbe and D.B.Young. 'X-ray structure analysis of the iron-dependent superoxide dismutase from Mycobacterium tuberculosis at 2.0 Ångstroms resolution reveals novel dimer-dimer interactions'. J.Mol.Biol. (1995) 246, 531-544.

J.B.Cooper, S.Saward, P.T.Erskine, M.O.Badasso, S.P.Wood, Y.Zhang and D.Young. 'X-ray structure analysis of an engineered Fe-superoxide dismutase Gly-Ala mutant with significantly reduced stability to denaturant'. FEBS Lett. (1996) 387, 105-108.

G.V.Louie, P.D.Brownlie, R.Lambert, J.B.Cooper, T.L.Blundell, S.P.Wood, V.N.Maleshkevich, A.Hadener, M.J.Warren and P.Shoolingin-Jordan. 'The three dimensional structure of Eschericia coli porphobilinogen deaminase at 1.76 Å resolution'. Proteins: Structure, Function and Genetics (1996) 25, 48-78.

Senior N., Thomas, P.G., Cooper, J.B., Wood, S.P., Erskine, P.T., Shoolingin-Jordan, P.M., Warren, M.J. 'Comparative studies of the 5-aminolevulinic acid dehydratase from P.sativum, E. coli and S. cerevisiae'. Biochem. J. (1996) 320, 401-412.

C.F.Aguilar, N.B.Cronin, M.Badasso, T.Dreyer, M.P.Newman, J.B.Cooper, D.J.Hoover, S.P.Wood, M.S.Johnson and T.L.Blundell. 'The three-dimensional structure at 2.4 Å resolution of glycosylated proteinase A from the lysosome-like vacuole of S. cerevisiae' J.Mol.Biol. (1997) 267, 899-915.

Erskine, P.T., Senior, N., Maignan, S., Cooper, J., Lambert, R., Lewis, G., Spencer, P., Awan, S., Warren, M., Tickle, I.J., Thomas, P., Wood, S.P. and Shoolingin-Jordan, P.M. 'Crystallisation of 5-aminolaevulinic acid dehydratase from Escherichia coli and Saccharomyces cerevisiae and preliminary X-ray characterisation of the crystals'. Pro. Sci. (1997) 6, 1774-1776.

P.T.Erskine, N.Senior, S.Awan, R.Lambert, G.Lewis, I.J.Tickle, M.Sarwar, P.Spencer, P.Thomas, M.J.Warren, P.M.Shoolingin-Jordan, S.P.Wood, and J.B.Cooper. 'X-ray structure analysis of 5-aminolaevulinate dehydratase, a hybrid aldolase. Nature Structural Biology (1997) 4, 1025-1031.

K.Bunting, J.Cooper, M.Badasso, I.J.Tickle, M.Newton, S.Wood, Y.Zhang and D.Young. Engineering a Change in Metal Ion Specificity of the Iron-Dependent Superoxide Dismutase from Mycobacterium tuberculosis: X-Ray Structure Analysis of Site-Directed Mutants. Eur. J. Biochem. (1998) 251, 795-803

S.J.Jackson and J.B.Cooper. 'An analysis of structural similarity in the iron and manganese superoxide dismutases based on known structures and sequences.' Biometals (1998) 11, 159-173.

'An epitope delivery system using recombinant mycobacteria' C.Hetzel, R.Janssen, S.J.Ely, N.M.Kristensen, K.Bunting, J.B.Cooper, J.R.Lamb, D.B.Young and J.E.R.Thole. Infect. Immun. (1998) 66, 3643-3648.

'Lead poisoning, haem synthesis and 5-aminolaevulinic acid dehyratase'. M.J.Warren, J.B.Cooper, S.P.Wood and P.M.Shoolingin-Jordan. TIBS (1998) 23, 217-221.

'X-ray structure of 5-aminolaevulinate dehydratase from Escherichia coli complexed with the inhibitor laevulinic acid at 2.0 Å resolution'. P.T.Erskine, E.Norton, J.B.Cooper, R.Lambert, A.Coker, G.Lewis, P.Spencer, M.Sarwar, S.P.Wood, M.J.Warren and P.M.Shoolingin-Jordan. Biochemistry (1999), 38, 4266-4276.

'The molecular structure of an unusual cytochrome c2 determined at 2.0 Å resolution; the cytochrome cH from Methylobacterium extorquens. J. Read, R. Gill, S.L. Dales, J.B. Cooper, S.P. Wood and C. Anthony. Protein Science (1999) 8, 1232-1240.

'The Schiff-base complex of yeast 5-aminolaevulinic acid dehydratase with laevulinic acid.' P.T. Erskine, R. Newbold, J. Roper, A. Coker, M.J. Warren, P.M. Shoolingin-Jordan, S.P. Wood and J.B. Cooper. Protein Science (1999), 1250-1256.

'High resolution crystal structure of a Mg2+ - dependent porphobilinogen synthase.' N. Frankenberg, P.T. Erskine, J.B. Cooper, P.M. Shoolingin-Jordan, D. Jahn and D.W. Heinz. J. Mol. Biol. (1999) J. Mol. Biol. (1999) 289, 591-602.

'Crystal structure of cardosin A, a glycosylated and Arg-Gly-Asp containing aspartic proteinase from the flowers of Cynara cardunculus L.' C. Frazao, I. Bento, J. Costa, C.M. Soares, P. Vérissimo, C. Faro, E. Pires, J.B. Cooper and M.A. Carrondo. J. Biol. Chem. (1999), 274, 27694-27701.

'A preliminary neutron Laue study of the aspartic proteinase endothiapepsin.' J.B. Cooper and D.A.A. Myles. Acta Crystallogr. (2000), D56, 246-248.

'MAD analyses of yeast 5-aminolaevulinate dehydratase. Their use in structure determination and in defining the metal binding sites.' P.T. Erskine, E.M.H. Duke, I.J. Tickle, N. Senior, M.J.Warren and J.B. Cooper. Acta Crystallogr. D. (2000), D56, 421-430.

'Purification, co-crystallization and preliminary X-ray analysis of the natural aspartic proteinase inhibitor IA3 complexed with saccharopepsin from Saccharomyces cerevisiae.' M. O. Badasso, J. A. Read, V. Dhanaraj, J. B. Cooper, S. P. Wood, T. L., Blundell, T. Dreyer and J. Winther. Acta Crystallogr. (2000) D56, 915-917.

'X-ray structures of five renin inhibitors bound to saccharopepsin: exploration of active-site specificity.' N.B. Cronin, M. O. Badasso, I. J.Tickle, T. Dreyer, D. J. Hoover, R. L. Rosati, C. C. Humblet, E. A. Lunney and J. B. Cooper. J. Mol. Biol. (2000), 303, 745-760.

'Site-directed mutagenesis and X-ray crystallography of the PQQ-containing quinoprotein methanol dehydrogenase and its electron acceptor cytochrome cL.' P. R. Afolabi, F. Mohammed, K. Amaratunga, O. Majekodunmi, S. L. Dales, R. Gill, D. Thompson, J. B. Cooper, S. P. Wood, P. M. Goodwin and C. Anthony (2001). Biochemistry 40, 9799-9809.

'The X-ray structure of yeast 5-aminolaevulinic acid dehydratase complexed with substrate and three inhibitors.' P. T. Erskine, R. Newbold, A. A. Brindley, S. P. Wood, P. M. Shoolingin-Jordan, M. J. Warren and J. B. Cooper (2001). J. Molec. Biol. 312, 133-141.

'The X-ray structure of yeast 5-aminolaevulinic acid dehydratase complexed with two diacid inhibitors.' P. T. Erskine, L. Coates, R. Newbold, A. A. Brindley, F. Stauffer, S. P. Wood, M. J. Warren, J. B. Cooper, P. M. Shoolingin-Jordan and R. Neier (2001). FEBS Lett. 503, 196-200.

'A neutron Laue diffraction study of endothiapepsin: implications for the aspartic proteinase mechanism.' L. Coates, P. T. Erskine, S. P. Wood, D. A. A. Myles and J. B. Cooper (2001). Biochemistry 40, 13149-13157.

'Engineering of an intersubunit disulphide bridge in the iron-dependent superoxide dismutase of Mycobacterium tuberculosis.' K. A. Bunting, J. B. Cooper, I. J. Tickle and D. B. Young (2002). Arch. Biochem. Biophys. 397, 69-76.

'Five atomic resolution structures of endothiapepsin inhibitor complexes: implications for the aspartic proteinase mechanism.' L. Coates, P. T. Erskine, M. P. Crump, S. P. Wood and J. B. Cooper (2002). J. Molec. Biol. 318, 1405-1415.

'The structure of endothiapepsin complexed with a gem-diol inhibitor PD-135,040 at 1.37 Å resolution.' L. Coates, P. T. Erskine, S. Mall, P. A. Williams, B. S. Gill, S. P. Wood and J. B. Cooper (2002). Acta Crystallogr. D 59, 978-981.

'X-ray structure of a putative reaction intermediate of 5-aminolaevulinic acid dehydratase.' Erskine, P. T., Coates, L., Butler, D., Youell, J. H., Brindley, A. A., Wood, S. P., Warren, M. J., Shoolingin-Jordan, P. M., Cooper, J. B. (2003) Biochem. J. 373, 733-738.

'Atomic resolution analysis of the catalytic site of an aspartic proteinase and an unexpected mode of binding by short peptides.' Erskine, P. T., Coates, L., Mall, S., Gill, R. S., Wood, S. P., Myles, D. A. A., Cooper, J. B. (2003) Protein Science 12, 1741-1749.